

CLAIMS

What is claimed is:

1. An isolated polynucleotide that encodes a cytokine polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 23 (Pro), to amino acid number 167 (Ile);

(b) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 1 (Met), to amino acid number 167 (Ile); and

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 179 (Ile); and

wherein the polypeptide produced by the cell induces proliferation of cells expressing a receptor for the polypeptide comprising zcytor11 (SEQ ID NO:19) or induces cytotoxicity in K562 cells.

2. An isolated polynucleotide according to claim 1, wherein the polynucleotide is selected from the group consisting of:

(a) a polynucleotide sequence as shown in SEQ ID NO:1 from nucleotide 123 to nucleotide 557;

(b) a polynucleotide sequence as shown in SEQ ID NO:1 from nucleotide 57 to nucleotide 557;

(c) a polynucleotide sequence as shown in SEQ ID NO:1 from nucleotide 21 to nucleotide 557; and

(d) a polynucleotide sequence complementary to (a), (b) or (c).

3. An isolated polynucleotide sequence according to claim 1, wherein the polynucleotide comprises nucleotide 1 to nucleotide 501 of SEQ ID NO:4.

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4. An isolated polynucleotide according to claim 1, wherein the cytokine polypeptide comprises a sequence of amino acid residues selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 23 (Pro), to amino acid number 167 (Ile);

(b) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 1 (Met), to amino acid number 167 (Ile); and

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 179 (Ile).

5. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA segment encoding a cytokine polypeptide as shown in SEQ ID NO:3 from amino acid number 23 (Pro), to amino acid number 167 (Ile); and

a transcription terminator,

wherein the promoter is operably linked to the DNA segment, and the DNA segment is operably linked to the transcription terminator.

6. An expression vector according to claim 5, further comprising a secretory signal sequence operably linked to the DNA segment.

7. A cultured cell comprising an expression vector according to claim 5, wherein the cell expresses a polypeptide encoded by the DNA segment.

8. A DNA construct encoding a fusion protein, the DNA construct comprising:

a first DNA segment encoding a polypeptide comprising a sequence of amino acid residues selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 1 (Met), to amino acid number 21 (Ala);

(b) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 41 (Thr), to amino acid number 53 (Leu);

(c) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 80 (Met), to amino acid number 91 (Val);

(d) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 103 (Gln), to amino acid number 116 (Arg);

(e) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 149 (Ile), to amino acid number 162 (Leu); and

(f) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 23 (Pro), to amino acid number 167 (Ile); and

at least one other DNA segment encoding an additional polypeptide, wherein the first and other DNA segments are connected in-frame; and wherein the first and other DNA segments encode the fusion protein.

9. An expression vector comprising the following operably linked elements:

a transcription promoter;

a DNA construct encoding a fusion protein according to claim 8; and

a transcription terminator,

wherein the promoter is operably linked to the DNA construct, and the DNA construct is operably linked to the transcription terminator.

10. A cultured cell comprising an expression vector according to claim 9, wherein the cell expresses a polypeptide encoded by the DNA construct.

11. A method of producing a fusion protein comprising:

culturing a cell according to claim 10; and

isolating the polypeptide produced by the cell.

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12. An isolated cytokine polypeptide comprising a sequence of amino acid residues that is at least 90% identical to an amino acid sequence selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 23 (Pro), to amino acid number 167 (Ile);

(b) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 1 (Met), to amino acid number 167 (Ile); and

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 179 (Ile); and

wherein the polypeptide produced by the cell induces proliferation of cells expressing a receptor for the polypeptide comprising zcytor11 (SEQ ID NO:19) or induces cytotoxicity in K562 cells.

13. An isolated polypeptide according to claim 12, wherein the polypeptide comprises a sequence of amino acid residues selected from the group consisting of:

(a) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 23 (Pro), to amino acid number 167 (Ile);

(b) the amino acid sequence as shown in SEQ ID NO:3 from amino acid number 1 (Met), to amino acid number 167 (Ile); and

(c) the amino acid sequence as shown in SEQ ID NO:2 from amino acid number 1 (Met), to amino acid number 179 (Ile).

14. A method of producing a cytokine polypeptide comprising:
culturing a cell according to claim 7; and
isolating the cytokine polypeptide produced by the cell.

15. A method of producing an antibody to a polypeptide comprising:
inoculating an animal with a polypeptide selected from the group consisting

of:

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(a) a polypeptide consisting of 30 to 144 amino acids, wherein the polypeptide is identical to a contiguous sequence of amino acids in SEQ ID NO:3 from amino acid number 23 (Gly) to amino acid number 779 (Thr);

(b) a polypeptide according to claim 13;

(c) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 29 (Arg) to amino acid number 34 (Asn);

(d) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 121 (His) to amino acid number 126 (Asp);

(e) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 134 (Gln) to amino acid number 139 (Thr);

(f) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 137 (Lys) to amino acid number 142 (Lys);

(g) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 145 (Glu) to amino acid number 150 (Lys);

(h) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 41 (Thr), to amino acid number 53 (Leu);

(i) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 80 (Met) to amino acid number 91 (Val);

(j) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 103 (Met) to amino acid number 116 (Arg);

(k) a polypeptide consisting of the amino acid sequence of SEQ ID NO:3 from amino acid number 149 (Ile) to amino acid number 162 (Leu); and

wherein the polypeptide elicits an immune response in the animal to produce the antibody; and

isolating the antibody from the animal.

16. An antibody produced by the method of claim 15, which binds to a polypeptide of SEQ ID NO:2 or SEQ ID NO:3.

17. The antibody of claim 16, wherein the antibody is a monoclonal antibody.

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18. An antibody that specifically binds to a polypeptide of claim 13.

19. A method of detecting, in a test sample, the presence of an antagonist of ZCYTO18 protein activity, comprising:

culturing a cell that is responsive to a ZCYTO18-stimulated cellular pathway;

and

producing a polypeptide by the method of claim 14; and

exposing the polypeptide to the cell, in the presence and absence of a test

sample; and

comparing levels of response to the polypeptide, in the presence and absence of the test sample, by a biological or biochemical assay; and

determining from the comparison, the presence of the antagonist of ZCYTO18 activity in the test sample.

20. A method of detecting, in a test sample, the presence of an agonist of ZCYTO18 protein activity, comprising:

culturing a cell that is responsive to a ZCYTO18-stimulated cellular pathway;

and

adding a test sample; and

comparing levels of response in the presence and absence of the test sample,

by a biological or biochemical assay; and

determining from the comparison, the presence of the agonist of ZCYTO18 activity in the test sample.

21. A method for detecting a genetic abnormality in a patient, comprising:

obtaining a genetic sample from a patient;

producing a first reaction product by incubating the genetic sample with a polynucleotide comprising at least 14 contiguous nucleotides of SEQ ID NO:1 or the complement of SEQ ID NO:1, under conditions wherein said polynucleotide will hybridize to complementary polynucleotide sequence;

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~~visualizing the first reaction product; and
 comparing said first reaction product to a control reaction product from a wild type patient,
 wherein a difference between said first reaction product and said control reaction product is
 indicative of a genetic abnormality in the patient.~~

22. A method for detecting a cancer in a patient, comprising:
 obtaining a tissue or biological sample from a patient;
 incubating the tissue or biological sample with an antibody of claim 18 under
 conditions wherein the antibody binds to its complementary polypeptide in the tissue or
 biological sample;
 visualizing the antibody bound in the tissue or biological sample; and
 comparing levels of antibody bound in the tissue or biological sample from the
 patient to a normal control tissue or biological sample,
 wherein an increase or decrease in the level of antibody bound to the patient
 tissue or biological sample relative to the normal control tissue or biological sample is
 indicative of a cancer in the patient.

~~23. A method for detecting a cancer in a patient, comprising:
 obtaining a tissue or biological sample from a patient;
 labeling a polynucleotide comprising at least 14 contiguous nucleotides of
 SEQ ID NO:1 or the complement of SEQ ID NO:1;
 incubating the tissue or biological sample with under conditions wherein the
 polynucleotide will hybridize to complementary polynucleotide sequence;
 visualizing the labeled polynucleotide in the tissue or biological sample; and
 comparing the level of labeled polynucleotide hybridization in the tissue or
 biological sample from the patient to a normal control tissue or biological sample,
 wherein an increase or decrease in the labeled polynucleotide hybridization to
 the patient tissue or biological sample relative to the normal control tissue or biological
 sample is indicative of a cancer in the patient.~~

24. A method of killing cancer cells comprising,

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obtaining *ex vivo* a tissue or biological sample containing cancer cells from a patient, or identifying cancer cells *in vivo*;

producing a polypeptide by the method of claim 14;

formulating the polypeptide in a pharmaceutically acceptable vehicle; and

administering to the patient or exposing the cancer cells to the polypeptide;

wherein the polypeptide kills the cells.

25. A method of killing cancer cells of claim 24, wherein the polypeptide is further conjugated to a toxin.

26. A method of increasing platelets in a patient or injured tissue,

producing a polypeptide by the method of claim 14;

administering the polypeptide to the patient or injured tissue in a pharmaceutically acceptable vehicle,

wherein the polypeptide increases the level of platelets in the patient or injured tissue.

27. A method for detecting inflammation in a patient, comprising:

obtaining a tissue or biological sample from a patient;

incubating the tissue or biological sample with an antibody of claim 18 under conditions wherein the antibody binds to its complementary polypeptide in the tissue or biological sample;

visualizing the antibody bound in the tissue or biological sample; and

comparing levels of antibody bound in the tissue or biological sample from the patient to a normal control tissue or biological sample,

wherein an increase in the level of antibody bound to the patient tissue or biological sample relative to the normal control tissue or biological sample is indicative of inflammation in the patient.

28. A method for detecting inflammation in a patient, comprising:

obtaining a tissue or biological sample from a patient;

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labeling a polynucleotide comprising at least 14 contiguous nucleotides of SEQ ID NO:1 or the complement of SEQ ID NO:1;

incubating the tissue or biological sample with under conditions wherein the polynucleotide will hybridize to complementary polynucleotide sequence;

visualizing the labeled polynucleotide in the tissue or biological sample; and

comparing the level of labeled polynucleotide hybridization in the tissue or biological sample from the patient to a normal control tissue or biological sample,

wherein an increase in the labeled polynucleotide hybridization to the patient tissue or biological sample relative to the normal control tissue or biological sample is indicative of inflammation in the patient.

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